510(k) SUBSTANTIAL EQUIVALENCE DETERMINATION
DECISION SUMMARY
DEVICE ONLY TEMPLATE

A. 510(k) Number: k033360

B. Analyte: Lithium

C. Type of Test: Quantitative Enzymatic Assay

D. Applicant: General Atomics

E. Proprietary and Established Names: Proprietary - Diazyme Lithium Enzymatic Assay, **Established –** Lithium enzymatic assay

F. Regulatory Information:

1. Regulation section: 21 CFR 862.3560

2. Classification: Class II

3. Product Code: JII

4. Panel: 91

G. Intended Use:

1. Intended use(s): Diazyme Lithium Enzymatic Assay Kit is for quantitative in vitro determination of lithium in human serum.

2. Indication(s) for use: Diazyme Lithium Enzymatic Assay Kit is for quantitative in vitro determination of lithium in human serum. Measurements of lithium are carried out essentially to ensure that the proper drug dosage is administered in the treatment of patients suffering from bipolar disorder and to avoid toxicity

3. Special condition for use statement(s): No special conditions were stated.

4. Special instrument Requirements: Roche Cobas Mira and Hitachi 717

H. Device Description: The Diazyme lithium assay is determined spectrophotmetrically through a kinetic coupling assay system involving a proprietary Phosphatase. Through enzymatic coupling, the phosphate is converted to hypoxanthine and generates hydrogen peroxide which in the presence of peroxidase forms a quinine dye with an absorbance of 556nm.

I. Substantial Equivalence Information:

1. Predicate device name(s): Trace Lithium Test System

2. Predicate K number(s): k003583

3. Comparison with predicate:

Similarities		
Item	**Device**	**Predicate**
Principle	Diazyme Enzymatic Colorimetric	Trace colorimetric
Type of test	Quantitative	Quantitative
Specimen type	Human Serum	Human Serum and Plasma
Reagent	Two reagent system	One reagent system

J. Standard/Guidance Document Referenced (if applicable): NCCLS EP5-A

K. Test Principle: Enzymatic colorimetric

L. Performance Characteristics (if/when applicable):

1. Analytical performance:

a. Precision/Reproducibility: The Diazyme Lithium Enzymatic assay was evaluated at two laboratories. In each run, low control serum sample containing 1.0 mM lithium and high control containing 2.2 mM lithium were analyzed. Within run precision @ 1mM Lithium 20 days, n=80, mean = 1.0mM, C.V.= 4.7%. Within run precision @ 2.3mM Lithium 20 days n=80, mean = 2.2, C.V = 3.3%. Total precision @ 1mM Lithium 20 days, n=80, mean = 1.0mM, C.V = 6.9%. Total precision @ 2.2 mM Lithium 20 days n=80, mean = 2.2, C.V = 5.5%.

b. Linearity/assay reportable range: Lithium free serum samples spiked with 1 M lithium acetate ranging from 0mM to 5mM were tested on UV-visible spectrophotometer and automated analyzers. The linearity of the Diazyme Lithium assay is 0.1 mM to 3.0 mM.

c. Traceability (controls, calibrators, or method): Serum calibrators 0mM, 1mM and 3mM are prepared by spiking lithium free serum with a 1mM lithium acetate stock solution

d. *Detection limit:* When testing serum samples between 0.1 mM to 3 mM lithium levels analytical recovery range ranged from 94 – 107%.

e. Analytical specificity: To determine the level of interference from other cations and substances normally present in the serum, the Diazyme Lithium Assay was tested with 1.0 mM lithium serum spiked with a variety of concentration of substances. The following cations and substances normally present in the serum reduced less than 10% deviation when tested at levels equal t the following concentrations – NH4 – 0.5 mM, Pi - 1.5 mM, Ca – 5mM, Na – 200 mM, K – 10 mM, Cu – 0.25 mM, Fe – 0.25 mM, Zn – 0.25 mM, Triglyceride 250 mg/dl, Ascorbic Acid – 5mM, Bilirubin - 45mg/dl.

f. Assay cut-off: The assay cutoff is established as the linear range of the Diazyme Lithium Assay (0.1mM – 3.0mM).

2. Comparison studies:

   a. Method comparison with predicate device: The correlation of the Diazyme Lithium Assay was evaluated against the predicate. N=61 slope = 0.94 and r=0.97 intercept = 0.1

   b. Matrix comparison:

3. Clinical studies:

   a. Clinical sensitivity:

   b. Clinical specificity:

   c. Other clinical supportive data (when a and b is not applicable):

4. Clinical cut-off:

5. Expected values/Reference range:

   A trough concentration for 12 hours post dose is expected to be 1.0 -1.2 mM. Levels higher than 1.5 nM, 12 hours after a dose indicates a significant risk of intoxication. Referenced to N. Tietz. Textbook of Clinical Chemistry, p. 1841. W.B. Saunders Company, Philadelphia (1986).

   The recommendation is made in the labeling that the above values should serve as reference only. Each laboratory should verify this range for the population it serves.

M. Conclusion: Based upon the information provided, I recommend that the Diazyme Lithium Enzymatic Assay be found substantially equivalent with the predicate devices as defined in 21 CFR 862.3560.